Association of Aortic Stiffness With Left Ventricular Remodeling and Reduced Left Ventricular Function Measured by Magnetic Resonance Imaging: The Multi-Ethnic Study of Atherosclerosis

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Background—This study sought to assess cross-sectional associations of aortic stiffness assessed by magnetic resonance imaging with left ventricular (LV) remodeling and myocardial deformation in the Multi-Ethnic Study of Atherosclerosis (MESA).

Methods and Results—Aortic arch pulse wave velocity (PWV) was measured with phase contrast cine magnetic resonance imaging. LV circumferential strain (Ecc), torsion, and early diastolic strain rate were determined by tagged magnetic resonance imaging. Multivariable linear regression models were used to adjust for demographics and cardiovascular risk factors. Of 2093 participants, multivariable linear regression models demonstrated that higher arch PWV was associated with higher LV mass index ($B=0.53$ per 1 SD increase for log-transformed PWV, $P<0.05$) and LV mass to volume ratio ($B=0.015$, $	ext{P}<0.01$), impaired LV ejection fraction (LVEF; $B=−0.84$; $P<0.001$), Ecc ($B=0.55$; $P<0.001$), torsion ($B=−0.11$; $P<0.001$), and early diastolic strain rate ($B=−0.003$; $P<0.05$). In sex stratified analysis, higher arch PWV was associated with higher MVR ($B=0.02$; $P<0.05$), impaired Ecc ($B=0.60$; $P<0.001$), and LVEF ($B=−0.45$; $P<0.05$), but with maintained torsion in women. Higher PWV was associated with impaired Ecc ($B=0.49$; $P<0.001$) and LVEF ($B=−1.21$; $P<0.001$), with lower torsion ($B=−0.17$; $P<0.001$) in men.

Conclusions—Higher arch PWV is associated with LV remodeling, and reduced LV systolic and diastolic function in a large multiethnic population. Greater aortic arch stiffness is associated with concentric LV remodeling and relatively preserved LVEF with maintained torsion in women, whereas greater aortic arch stiffness is associated with greater LV dysfunction demonstrated as impaired Ecc, torsion, and LVEF, with less concentric LV remodeling in men. (Circ Cardiovasc Imaging. 2016;9:e004426. DOI: 10.1161/CIRCIMAGING.115.004426.)

Key Words: epidemiology ■ heart ventricles ■ magnetic resonance imaging ■ pulse wave analysis ■ vascular stiffness

The central aorta serves as a conduit to deliver blood to peripheral organs and also as a cushion to buffer the pulsatile pressure and flow from the heart. A stiffened aorta has less buffering effect on pulsatile pressure leading to increased left ventricular (LV) afterload. Therefore, arterial stiffness is associated with the incidence of cardiovascular disease.1–3

See Editorial by O’Regan See Clinical Perspective

Magnetic resonance imaging (MRI) has the unique ability to combine the assessment of ventricular geometry, myocardial function, and central aortic stiffness in a single examination. Regional pulse wave velocity (PWV) in the thoracic aorta can be assessed by MRI with a great level of accuracy and reproducibility.4–9 PWV measured by MRI has several advantages, such as full 3-dimensional visualization of the vessel, allowing for accurate measurements compared with standard carotid-femoral PWV.6 Cardiovascular magnetic resonance (CMR) is currently considered as the gold standard for assessing myocardial structure and tagged CMR provides precise quantification of myocardial deformation parameters including myocardial strain and torsion.7,8
The impact of aortic stiffness on LV geometry and performance is important from public health and therapeutic viewpoints. Identifying an association between increased aortic stiffness and impaired myocardial deformation parameters may elucidate potential mechanisms for impaired vascular–ventricular coupling in the pathogenesis of heart failure (HF). Although several studies have explored the association of aortic stiffness and global ventricular dysfunction in hypertension participants and the general population, no studies have explored the association between aortic stiffness assessed by MRI and myocardial deformation in a large general population cohort. Thus, in the present study, we aim to determine the relationship of aortic arch PWV with LV remodeling (LV mass and volume) and LV function including myocardial deformation parameters (LV ejection fraction [EF], circumferential strain, torsion, and early diastolic strain rate) in a large multiethnic cohort. We also aim to determine whether any of these associations are sex-specific because previous studies have shown that there are sex differences in LV structure and function as well as in arterial stiffness.1,12

Methods

Study Population

The Multi-Ethnic Study of Atherosclerosis has been previously described.13 In summary, it is a population-based sample of 6814 men and women aged 45 to 84 years without clinical cardiovascular disease at the time of enrollment who identified themselves as white, black, Hispanic, or Chinese from 6 US communities (Baltimore, New York, Minneapolis, Winston-Salem, Los Angeles, and Chicago). In the longitudinal follow-up (fifth examination) of subjects in the MESA study from 2010 to 2012, a total of 3026 participants underwent CMR imaging. Of these, 2227 participants had aortic MRI and CMR imaging performed as part of the scans. After excluding 134 participants because of bad image quality mainly by motion artifact, 2093 participants (94% of all available aortic MRI) were included for this study. All participants gave informed consent with breath hold. These images allow us to measure the distance between ascending and descending aorta was measured at precise locations where the through velocities were measured (Figure 1). Aortic arch PWV was then calculated as follows:

$$\text{PWV} (m/s) = \frac{\text{distance (mm)}}{\text{transit time (between ascending to descending (ms))}}$$

Higher aortic arch PWV represents greater aortic stiffness. Intra- and interobserver reproducibility of arch PWV was excellent with an intraaclass correlation coefficient ranging 0.94 to 0.99.2

CMR cine and tagging imaging were performed to assess LV mass, volumes, LVEF, and deformation parameters as previously described.16 LV mass and LV volumes were indexed to height13,17 Average peak midventricular midwall circumferential strain (Ecc) is a negative value and more negative values indicate greater circumferential shortening. Ecc was calculated by averaging the corresponding midventricular peak segmental strain values from 4 ventricular segments16 (Figure 2). LV torsion was defined by LV twist normalized by slice distance.17 Early diastolic strain rate (EDSR) was identified as the first peak in the diastolic phase of the circumferential strain rate curve.19

Cardiovascular Disease Risk Factors Assessment

During the fifth examination follow-up period in MESA, participants completed standardized questionnaires to provide information about demographic variables, smoking history, and medication usage. Resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the seated position using an automated oscillometric sphygmomanometer. Mean blood pressure (MBP) was calculated as (2×DBP+SBP)/3. Pulse pressure was calculated as (SBP–DBP). Hypertension was defined as SBP≥140 mmHg, DBP≥90 mmHg, or current use of antihypertensive medications. Glucose and lipids were measured after a 12-hour fast. Diabetes mellitus was defined as fasting glucose ≥126 mg/dL or use of insulin or oral hypoglycemic medications.

Statistical Analysis

Continuous variables are presented as means±SD for normally distributed data and median (25%ile, 75%ile) for non-normally distributed data. Categorical variables are presented as frequencies and percentages. Comparisons of LV data and PWV between genders were performed using Student t tests and Mann–Whitney U test for normally and non-normally distributed data, respectively. PWV was logarithmically transformed for linear regression models and figure because of non-normally distribution.

The associations of aortic arch PWV with LV structure (LV mass, volumes, LVEF, torsion, and EDSR) variables were assessed using multivariable linear regression analysis, with LV variables as dependent variables. The models adjusted for the following covariates: demographics (age, sex, and ethnicity), traditional cardiovascular risk factors—SBP, antihypertensive medication use, diabetes mellitus, obesity (body mass index>30), heart rate, low-density lipoprotein, high-density lipoprotein and current smoking status—and the presence of cardiovascular disease. For the LV functional variables, models further adjusted for LV mass and volume to volume ratio (LVMVR) and function (LVEF, Ecc, torsion, and EDSR) variables were assessed using multivariable linear regression analysis, with LV variables as dependent variables. The models adjusted for the following covariates: demographics (age, sex, and ethnicity), traditional cardiovascular risk factors—SBP, antihypertensive medication use, diabetes mellitus, obesity (body mass index>30), heart rate, low-density lipoprotein, high-density lipoprotein and current smoking status—and the presence of cardiovascular disease. For the LV functional variables, models further adjusted for LV mass and volume to volume ratio (LVMVR) and function (LVEF, Ecc, torsion, and EDSR) variables were assessed using multivariable linear regression analysis, with LV variables as dependent variables.

Results

MESA Participants’ Characteristics

Table 1 shows baseline the study participants’ demographics and clinical and MRI variables. The study population was 47%...
men, 40% white, 14% Chinese American, 26% black, and 20% Hispanic; 59% were hypertensive; 18% had diabetes mellitus; and 7% were active smokers with mean age of 69.5±9.4 years. At the time of the examination, 29 participants had HF, 42 had myocardial infarction, and 74 had angina pectoris over the 10 years of follow-up. Median value of arch PWV was 8.0 (6.4, 10.0) m/s (Figure I in the Data Supplement).

Association of LV Structure and Function With Aortic Stiffness

Table 2 shows the association of LV structure and function with aortic arch PWV. Higher PWV was associated with lower LV end-diastolic volume index, higher LV mass index, and LVMVR in univariate regression analysis. The associations of greater PWV with LV mass index ($B=0.53$ [95% confidence interval, 0.12–0.95] g/m$^2$ per 1 SD increase for log-transformed PWV; $P<0.05$) and LVMVR ($B=0.015$ [0.006–0.025] g/mL; $P<0.001$) remained significant after adjustment for traditional cardiovascular risk factors. With regard to LV functional variables, higher PWV was associated with impaired LVEF ($B=-0.84$ [−1.16 to −0.52] %; $P<0.001$), impaired Ecc ($B=0.55$ [0.40–0.69] %; $P<0.001$), lower torsion ($B=-0.11$ [−0.17 to −0.06] °/cm; $P<0.001$) and lower EDSR ($B=-0.003$ [−0.005 to −0.001]; $P<0.05$) in multivariable analysis. These associations of PWV with the impaired systolic function (EF, Ecc, and torsion) persisted even after adjustment for LV mass and LV end-diastolic volume, whereas the association of PWV with impaired LV diastolic function represented by reduced EDSR was absent after further adjustment for LV structural variables. These associations of PWV with LV measures were also maintained after further adjustment for aortic area as a potential confounder, except for the association with LV mass index that showed nonsignificant ($P=0.30$). Similar results were obtained in models using mean or diastolic pressure or pulse pressure instead of SBP (data not shown).

Sex-Specific Changes in LV Structure and Function With Increasing Aortic PWV

There was no significant difference in arch PWV between men and women. Men had significantly higher LV mass index, LV end-diastolic volume index, LV end-systolic volume index, and LVMVR (all $P<0.001$) than women. LV systolic function analysis showed impaired Ecc, torsion, EDSR, and LVEF (all $P<0.001$) in men compared with women (Table I in the Data Supplement). There was a significant interaction with sex in the association of aortic PWV with LV torsion ($B$ for interaction=−0.13 [−0.23 to −0.02] °/cm; $P=0.013$) and LVEF ($B$ for interaction=−0.77 [−1.36 to −0.19] %; $P=0.009$).

**Figure 1.** Measurement for aortic arch pulse wave velocity (PWV). A, Phase contrast cine transverse view. B, Aortic arch view with steady state free precession sequence. C, Measurement of the transit distance in the aortic arch. Numbers correspond to those in A and B. Arch length is measured as the distance from 3 to 11 in this case. D, Flow wave curves of ascending (Asc.) aorta and descending (Desc.) aorta after peak flow normalization. Transit time is measured as the average time difference using the least squares estimate between all data points on the systolic upslope of the ascending and descending aortic flow curves. PWV is calculated as transit distance divided by transit time.
Table 3 shows the sex-specific associations between arch PWV and LV structural and functional variables. Higher arch PWV was associated with higher LV mass index ($B=0.53 \ [0.03–1.03] \ g/m^{1.7}; P<0.05$) and LVMVR ($B=0.020 \ [0.009–0.032] \ g/mL; P<0.01$) after adjustment for traditional risk factors in women only, whereas no association with LV remodeling variables was found in men. In men, higher PWV was associated with impaired Ecc ($B=0.49 \ [0.27–0.70] \ %; P<0.001$), LV torsion ($B=−0.17 \ [−0.24 \ to −0.09] \ °/cm; P<0.001$), and LVEF ($B=−1.21 \ [−1.70 \ to −0.73] \ %; P<0.001$) after adjustment for traditional risk factors. In women, higher PWV was associated with impaired Ecc ($B=0.60 \ [0.39–0.80] \ %; P<0.001$), but torsion remained unchanged. Higher PWV was associated with reduced LVEF but was not pronounced in women ($B=−0.45 \ [−0.88 \ to −0.02] \ %; P<0.05$) compared with men. These associations of PWV with systolic functional variables persisted in both sexes after further adjustment for LV structural variables. In addition, higher PWV was associated with lower EDSR only in women after adjustment for traditional risk factors, but this relationship was absent after adjustment for LV remodeling factor. Further adjustment for
The present study demonstrates that higher aortic arch stiffness is associated with greater LV concentric remodeling, as demonstrated by the positive relationship with higher LV mass index and LVMVR. Furthermore, higher aortic arch PWV is associated with impaired LV systolic function as demonstrated by impaired Ecc and LV torsion as well as by impaired LVEF in a large multiethnic population. The association of PWV with lower EDSR, a marker of early diastolic dysfunction, was also demonstrated. These associations of PWV with altered myocardial deformation variables persisted after adjustment for traditional cardiovascular risk factors and measures of LV remodeling. In women, increasing arch PWV is associated with LV concentric remodeling, worse diastolic function, and relatively preserved systolic function, whereas progressive LV systolic dysfunction with less concentric remodeling was seen in men. To the best of our knowledge, the relationships of aortic stiffness by MRI with LV structure and function including myocardial deformation variables derived from MRI tagging have not been demonstrated previously, particularly in a large general population cohort.

The relationship between PWV and LV geometry has been explored extensively in hypertensive patients. Increased aortic stiffness results in increased cardiac afterload, inducing concentric remodeling. We found that arch PWV was positively correlated with both LV mass and LVMVR independent of blood pressure and other cardiovascular risk factors. These results are inconsistent with previous reports, which found that higher aortic PWV assessed by tonometry was associated with concentric remodeling as demonstrated by higher relative wall thickness using echocardiography, without a significant increase in LV mass. The difference in findings between previous studies might be a result of improved precision in both aortic and LV parameter assessment by MRI, the advantage of a larger population allowing for greater statistical power, and the difference in population variables derived from MRI tagging have not been demonstrated previously, particularly in a large general population cohort.

With the progressive stiffening of the elastic arteries, cardiac afterload increases because accelerated reflected wave returns earlier, during late systole, which augments the SBP and adds extra stress to the LV. Arterial stiffness is also associated with lower diastolic blood pressure and reduced coronary perfusion. Higher systolic work and a mismatch in the ratio between myocardial supply and oxygen demand could result in reduced cardiac systolic and diastolic performance. In addition, the recent study demonstrated that greater aortic stiffness is associated with reduced longitudinal stretch-related aortic work that might lead to lower early diastolic filling. In the present study, increased aortic arch PWV was associated with LV systolic and diastolic dysfunction. This finding is consistent with the previous study from MESA that showed the association of increased carotid artery stiffness assessed by ultrasound with impaired Ecc and LV torsion as measures for systolic function, adding to LVEF which is a marker for global systolic function. Increased PWV was accompanied by impaired Ecc.
Aortic stiffness and LV remodeling and function

Arch PWV was independently associated with LV systolic and diastolic dysfunction after adjustment for age, blood pressure, and other cardiovascular risk factors, supporting the hypothesis of a direct effect of increased aortic stiffness on LV function. The association of increased PWV with reduced EDSR was attenuated after adjustment for LV geometric measures, indicating that the development of concentric remodeling with increased aortic stiffness might induce LV diastolic dysfunction.

Table 2. Association of Log-Transformed Pulse Wave Velocity With LV Structural and Functional Variables

<table>
<thead>
<tr>
<th>Response</th>
<th>$R^2$</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDVi, mL/m$^{1.7}$</td>
<td>0.22</td>
<td>−0.75 (−1.22 to −0.28)*</td>
<td>−0.08 (−0.54 to 0.39)</td>
<td>…</td>
</tr>
<tr>
<td>LVESVi, mL/m$^{1.7}$</td>
<td>0.19</td>
<td>0.27 (−0.01 to 0.55)</td>
<td>0.46 (0.18 to 0.74)*</td>
<td>…</td>
</tr>
<tr>
<td>LVMi, g/m$^{1.7}$</td>
<td>0.46</td>
<td>0.92 (0.41 to 1.42)*</td>
<td>0.53 (0.12 to 0.95)†</td>
<td>…</td>
</tr>
<tr>
<td>LVMRV, g/mL</td>
<td>0.24</td>
<td>0.039 (0.030 to 0.049)‡</td>
<td>0.015 (0.006 to 0.025)*</td>
<td>…</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>0.23</td>
<td>−0.93 (−1.24 to −0.61)†</td>
<td>−0.84 (−1.16 to −0.52)‡</td>
<td>−0.86 (−1.17 to −0.55)‡</td>
</tr>
<tr>
<td>Ecc, %</td>
<td>0.25</td>
<td>0.69 (0.55 to 0.83)‡</td>
<td>0.55 (0.40 to 0.69)‡</td>
<td>0.48 (0.34 to 0.63)‡</td>
</tr>
<tr>
<td>Torsion, °/cm</td>
<td>0.27</td>
<td>−0.07 (0.12 to −0.01)†</td>
<td>−0.11 (−0.17 to −0.06)‡</td>
<td>−0.11 (−0.16 to −0.06)‡</td>
</tr>
<tr>
<td>EDSR, 1/s</td>
<td>0.12</td>
<td>−0.007 (−0.009 to −0.005)‡</td>
<td>−0.003 (−0.005 to −0.001)†</td>
<td>−0.002 (0.005 to 0.0002)</td>
</tr>
</tbody>
</table>

Coefficients and 95% confidence interval (in brackets) were estimated using multivariable linear regression models to assess the association of log-transformed pulse wave velocity (per 1 SD) with LV structural and functional variables as dependent variables. Model 1: unadjusted; model 2: adjusted for age, sex, race, smoking, diabetes mellitus, antihypertensive medication, obesity, systolic blood pressure, heart rate, low-density lipoprotein, high-density lipoprotein, and cardiovascular disease; model 3: adjusted for model 2 + LVMi and LVEDVi. Ecc indicates left ventricular circumferential strain; EDSR, early diastolic strain rate; LVEDVi, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume; LVMi, left ventricular mass indexed to height$^{1.7}$; and LVMRV, left ventricular mass volume ratio.

*if $P<0.01$, †if $P<0.05$, ‡if $P<0.001$.

and LV torsion, leading to depressed LV global systolic function. Arch PWV was independently associated with LV systolic and diastolic dysfunction after adjustment for age, blood pressure, and other cardiovascular risk factors, supporting the hypothesis of a direct effect of increased aortic stiffness on LV function. The association of increased PWV with reduced EDSR was attenuated after adjustment for LV geometric measures, indicating that the development of concentric remodeling with increased aortic stiffness might induce LV diastolic dysfunction.

Table 3. Sex-Specific Changes in LV Structure and Function With Log-Transformed Pulse Wave Velocity

<table>
<thead>
<tr>
<th>Response</th>
<th>$R^2$</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDVi, mL/m$^{1.7}$</td>
<td>0.25</td>
<td>−0.98 (−1.55 to −0.41)*</td>
<td>−0.27 (−0.81 to 0.28)</td>
<td>…</td>
</tr>
<tr>
<td>LVESVi, mL/m$^{1.7}$</td>
<td>0.13</td>
<td>−0.10 (−0.42 to 0.21)</td>
<td>0.17 (−0.15 to 0.49)</td>
<td>…</td>
</tr>
<tr>
<td>LVMi, g/m$^{1.7}$</td>
<td>0.38</td>
<td>0.75 (0.17 to 1.33)‡</td>
<td>0.53 (0.03 to 1.03)†</td>
<td>…</td>
</tr>
<tr>
<td>LVMRV, g/mL</td>
<td>0.24</td>
<td>0.042 (0.030 to 0.054)*</td>
<td>0.020 (0.009 to 0.032)*</td>
<td>…</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>0.10</td>
<td>−0.41 (−0.82 to −0.002)‡</td>
<td>−0.45 (−0.88 to −0.02)‡</td>
<td>−0.52 (−0.95 to −0.10)‡</td>
</tr>
<tr>
<td>Ecc, %</td>
<td>0.23</td>
<td>0.72 (0.52 to 0.91)*</td>
<td>0.60 (0.39 to 0.80)*</td>
<td>0.50 (0.31 to 0.70)*</td>
</tr>
<tr>
<td>Torsion, °/cm</td>
<td>0.17</td>
<td>−0.001 (−0.08 to 0.08)</td>
<td>−0.06 (−0.14 to 0.03)</td>
<td>−0.06 (−0.14 to 0.02)</td>
</tr>
<tr>
<td>EDSR, 1/s</td>
<td>0.11</td>
<td>−0.007 (−0.010 to −0.004)*</td>
<td>−0.0035 (−0.0068 to −0.0001)†</td>
<td>−0.002 (−0.006 to 0.001)</td>
</tr>
</tbody>
</table>

Men | | | | |
| LVEDVi, mL/m$^{1.7}$ | 0.15 | −0.80 (−1.51 to −0.08)‡ | 0.19 (−0.59 to 0.97) | … |
| LVESVi, mL/m$^{1.7}$ | 0.11 | 0.42 (−0.03 to 0.86) | 0.79 (0.30 to 1.28)† | … |
| LVMi, g/m$^{1.7}$ | 0.28 | 0.51 (−0.18 to 1.20) | 0.61 (−0.08 to 1.30) | … |
| LVMRV, g/mL | 0.16 | 0.030 (0.016 to 0.045)* | 0.010 (−0.005 to 0.026) | … |
| LVEF, % | 0.23 | −1.22 (−1.67 to −0.77)† | −1.21 (−1.70 to −0.73)* | −1.17 (−1.64 to −0.70)* |
| Ecc, % | 0.25 | 0.62 (0.42 to 0.82)* | 0.49 (0.27 to 0.70)* | 0.44 (0.24 to 0.65)* |
| Torsion, °/cm | 0.19 | −0.09 (0.15 to −0.02)† | −0.17 (−0.24 to −0.09)* | −0.16 (−0.23 to −0.09)* |
| EDSR, 1/s | 0.10 | −0.006 (−0.009 to −0.003)* | −0.002 (−0.006 to 0.001) | −0.002 (−0.005 to 0.002) |

Coefficients and 95% confidence interval (in brackets) were estimated using multivariable linear regression models to assess the association of log-transformed pulse wave velocity (per 1 SD) with LV structural and functional variables as dependent variables. Model 1: unadjusted; model 2: adjusted for age, race, smoking, diabetes mellitus, antihypertensive medication, obesity, systolic blood pressure, heart rate, low-density lipoprotein, high-density lipoprotein, and cardiovascular disease; model 3: adjusted for model 2 + LVMi and LVEDVi. Ecc indicates left ventricular circumferential strain; EDSR, early diastolic strain rate; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume; LVMi, left ventricular mass indexed to height$^{1.7}$; and LVMRV, left ventricular mass volume ratio.

*if $P<0.001$, †if $P<0.01$, ‡if $P<0.05$. 
Sex differences seem to exist in the vascular–ventricular interaction measured at the population level, with men developing greater global LV systolic dysfunction than women even though impaired Ecc was seen in both sexes with greater PWV. Previous studies demonstrated sex differences in cardiac remodeling with women having higher LV torsion than men. Torsion may act as a compensatory mechanism to maintain LVEF in the face of worse Ecc. In the present study, the maintained torsion in women would help to maintain LVEF with increasing PWV. Several previous studies have demonstrated that women are more likely to develop concentric remodeling with pressure overload compared with men. Congruent with previous studies, the present study identified that higher LVMVR, as an indicator of concentric remodeling, related to increasing PWV was pronounced only in women after adjustment for cardiovascular risk factors. In accordance with the lever-arm theory, a greater radius difference between the endocardium and the epicardium would result in increased torsion caused by a helical contraction effect. Greater LVMVR with greater PWV may contribute to maintain systolic function through maintained torsion among women in this study population. Studies have shown that greater LV fibrosis assessed by T1 mapping is associated with impaired Ecc and preserved LVEF in women, whereas in men, greater fibrosis is associated with impaired Ecc, LV torsion, and LVEF in the MESA population. Thus, aortic stiffness in association with LV fibrosis may also contribute to the difference in the association of PWV with LV deformation variables.

Previous studies have also demonstrated that women are more vulnerable to the development of HF with preserved EF. Whether the impact of arterial stiffness on diastolic function is different in men and women is also debated. In the present study, aortic arch PWV was associated with EDSR as an indicator of LV diastolic dysfunction only in women, independent of cardiovascular risk factors. The development of concentric LV geometry with increasing PWV in women might also induce lower relaxation because the relationship between PWV and EDSR was attenuated after adjustment for LV mass and left ventricular end-diastolic volume. Because both arterial stiffness and diastolic dysfunction have been proposed as possible factors involved in the pathogenesis of HF with preserved EF, impaired LV diastolic function as well as maintained systolic function with increasing PWV in woman may be a preclinical finding in the pathway to HF with preserved EF.

**Limitations**

The cross-sectional design of the study does not allow for the detection of cause–effect relationships, but only of associations between the studied variables. A causal link between aortic PWV and LV structure and function is suggested, but longitudinal studies are needed to confirm this hypothesis. Because our sample group was composed of older adults (52–92 years), it is not possible to generalize these results to younger adults. We might have inflated type I error because of multiple testing. We did not assess other variables such as augmentation index or reflected magnitude that represents wave reflections, besides PWV. Additional studies should be conducted to assess whether other factors related to aortic
stiffness influence LV structure and function. The strength of the present study is the large, community-based multiethnic sample of participants with detailed risk factor data and sophisticated MRI imaging data.

Conclusions
In our cross-sectional, community-based cohort study, greater aortic stiffness as demonstrated by increased aortic arch PWV was associated with reduced LV systolic and diastolic function and LV remodeling. With greater arch PWV, LV concentric remodeling, reduced LV diastolic function and relatively preserved EF accompanied with preserved torsion were seen in women, whereas reduced LV systolic function accompanied with reduced torsion and less LV remodeling were seen in men. Investigations are needed to assess the risk of future HF associated with increased arterial stiffness and the possible impact of therapeutic strategies aimed at improving arterial elasticity on the risk of subsequent HF.

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Disclosures
None.

Reference


**CLINICAL PERSPECTIVE**

The present study demonstrates a consistent association between aortic arch pulse wave velocity, as a marker of aortic stiffness, and impaired left ventricular function in a large multiethnic cohort. The present study also demonstrates sex-specific changes in left ventricular structure and function with increasing arch pulse wave velocity. By elucidating the presence of early vascular dysfunction in the setting of subclinical left ventricular dysfunction, this study provides evidence in support of novel paradigms for understanding the pathogenesis and the progression of heart failure.
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**SUPPLEMENTAL MATERIAL**

Supplemental Table. Aortic Stiffness and LV Variables Stratified by Gender

<table>
<thead>
<tr>
<th>Aortic Stiffness Parameter</th>
<th>Women (n=1110)</th>
<th>Men (n=983)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic arch PWV, m/s</td>
<td>7.9 (6.3 to 10.0)</td>
<td>8.0 (6.5 to 10.1)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>LV parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVMi, g/m(^{1.7})</td>
<td>46.5 ± 9.5</td>
<td>57.5 ± 11.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDVi, ml/m(^{1.7})</td>
<td>47.3 ± 9.4</td>
<td>52.5 ± 11.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESVi, ml/m(^{1.7})</td>
<td>17.5 ± 5.2</td>
<td>21.4 ± 7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVMVR, g/ml</td>
<td>1.00 ± 0.20</td>
<td>1.13 ± 0.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>64.0 ± 6.7</td>
<td>59.6 ± 7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ecc, %</td>
<td>-16.7 ± 3.3</td>
<td>-15.7 ± 3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Torsion, °/cm</td>
<td>4.6 ± 1.3</td>
<td>3.7 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EDSR, 1/s</td>
<td>0.120 ± 0.052</td>
<td>0.102 ± 0.050</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

p for women vs. men. Abbreviations as in Table 1.
Supplemental Figure. Histogram for Aortic Arch PWV